Research Article

A Simple and Convenient Method For the Synthesis of Pyrazole Derivatives Using Iron (III) Chloride Hexahydrate In Aqueous Media

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ABSTRACT

An efficient and convenient synthesis of 4,4'-(phenylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) derivatives has been achieved by one pot two-component condensation reaction of 3-methyl-1-phenyl-1*H*-pyrazol-5-ol (**2**) with substituted benzaldehydes (**2a-p**) in presence of of Iron(III) chloride hexahydrate in good to excellent yields.

Keywords: Iron(III) chloride hexahydrate, water, one pot two-component condensation.

INTRODUCTION

Recently, pyrazole derivatives have attained considerable significance as potential biological and pharmacological target heterocyclic compounds in medicinal chemistry and organic chemistry research.[1] The prime driving force in this area is the fight against antitubercular activity,[2] antipyretic activity,[3] gastric secretion stimulatory[4] antitumor activity,[5] antibacterial activity[6] antifilarial activity[7], and antidepressant[8] agents. These compounds have been also used as pesticides,[9] insecticides[10] and fungicides[11]

The construction of new analogs heterocyclic compounds represents a major challenge in synthetic organic and medicinal chemistry. Due to their broad spectrum of biological interest chemists have developed a few methods for the synthesis of pyrazole derivatives.[12] To the best of our knowledge, there are no reports on the use of $FeCl_3$-$6H_2O$ catalyst for this conversion. This fact has prompted us to investigate $FeCl_3$-$6H_2O$ for the synthesis of pyrazole derivatives in a facile and practical manner. Because of the toxic and volatile nature of many organic solvents, water as reaction medium was considered a very promising and attractive substitute for volatile organic solvents and was widely used in the green chemistry. There has been growing reorganization that water is an attractive medium for many organic reactions resulting in less expensive, less dangerous, and environmentally friendly reactions such as Diels-Alder reactions,[13] Claisen rearrangement reactions.[14] As part of our current studies on the development of new routes to heterocyclic systems,[15] we now report an efficient and clean synthetic route to pyrazole derivatives in aqueous medium catalyzed by $FeCl_3$-$6H_2O$ by the reaction of 3-methyl-1-phenyl-1*H*-pyrazol-5-ol with substituted aldehydes.

Recently iron has been increasingly explored in organic transformations as an inexpensive and environmentally benign catalyst.[16] $FeCl_3$-$6H_2O$ as a Lewis acid catalyst has been increasingly utilized in a wide variety of organic reactions such as the preparation of xanthenediones,[17] and Hantzsch 1,4-dihydropyridines,[18] Biginelli condensations,[19] and Beckmann rearrangements.[20] 4,4'-(phenylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) derivatives is still highly desirable in terms of developing more practical procedures and mild reaction conditions. As a consequence of our interest in developing new and efficient synthetic methodologies for the synthesis of organic compounds,[21-25] we report herein a convenient, mild and environmentally benign method for the preparation of 4,4'-(phenylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) by the condensation of 3-methyl-1-phenyl-1*H*-pyrazol-5-ol with substituted aldehydes using catalytic $FeCl_3.6H_2O$ at room temperature in aqueous media. To the best of our knowledge, the synthesis of 4,4'-(phenylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) catalyzed by $FeCl_3$-$6H_2O$ has not been reported.

RESULTS AND DISCUSSION

Initially, a model reaction was examined using 3-methyl-1-phenyl-1*H*-pyrazol-5-ol (**2**), benzaldehyde (**1**) and in the presence of

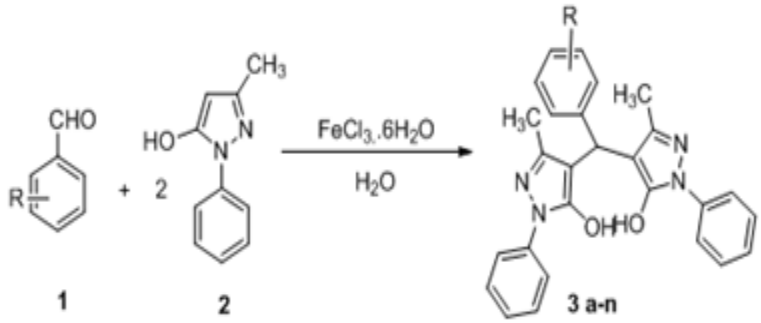
Iron(III) chloride hexahydrate (10 mol %) in water as solvent **(Scheme 1)**. After1 h 94 % of 4,4'-(phenylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) (**3**) product was isolated. When the amount of catalyst is increased to 30 mole %, there is no much variation in the yield. Subsequently, we investigated the effect of different solvents on the reaction and as well as yields of the product. **(Table 1)** The use of water resulted in higher yields than ethanol, *n*-butanol. *etc*., **(Table 1).**

Table 1: Effect of reaction media on the preparation of 3a from the electrophilic substitution reaction of 2 with benzaldehyde catalyzed by $FeCl_3$-6H_2O

S.No	Solvent	Time	Yield
1	MeOH	1 h	20%
2	EtOH	1 h	63%
3	$CHCl_3$	1 h	45%
4	CH_2Cl_2	1 h	48%
5	CCl_4	1 h	60%
6	Et_2O	1 h	40%
7	Toluene	1 h	56%
8	Benzene	1 h	58%
9	CH_3CN	1 h	78%
10	DMF	1 h	15%

With optimized conditions in hand, when the reaction of 3-methyl-1-phenyl-1*H*-pyrazol-5-ol with substituted aromatic aldehydes was performed in water, presence of $FeCl_3$-6H_2O at room temperature, high yields of pyrazole derivatives (**3a-n**) were obtained (**Scheme 1**). To apply this reaction to a library synthesis, various kinds of adehydes and 3-methyl-1-phenyl-1*H*-pyrazol-5-ol were subjected to give the corresponding pyrazole derivatives and representative examples are shown in **Scheme 1**. All the pyrazole derivatives were obtained in excellent yields with good purity. The isolated products were completely characterized by IR, ^{1}H NMR, ^{13}C NMR and Mass spectroscopic analysis. The formation of compound **3a** was evident from the appearance of $[M+H]^+$ peak at *m/z* 437 in mass spectrum (ESI), hydroxy stretching at 3423 cm^{-1} in IR and the characteristic benzylic proton at δ 4.72 as a singlet in ^{1}H NMR.

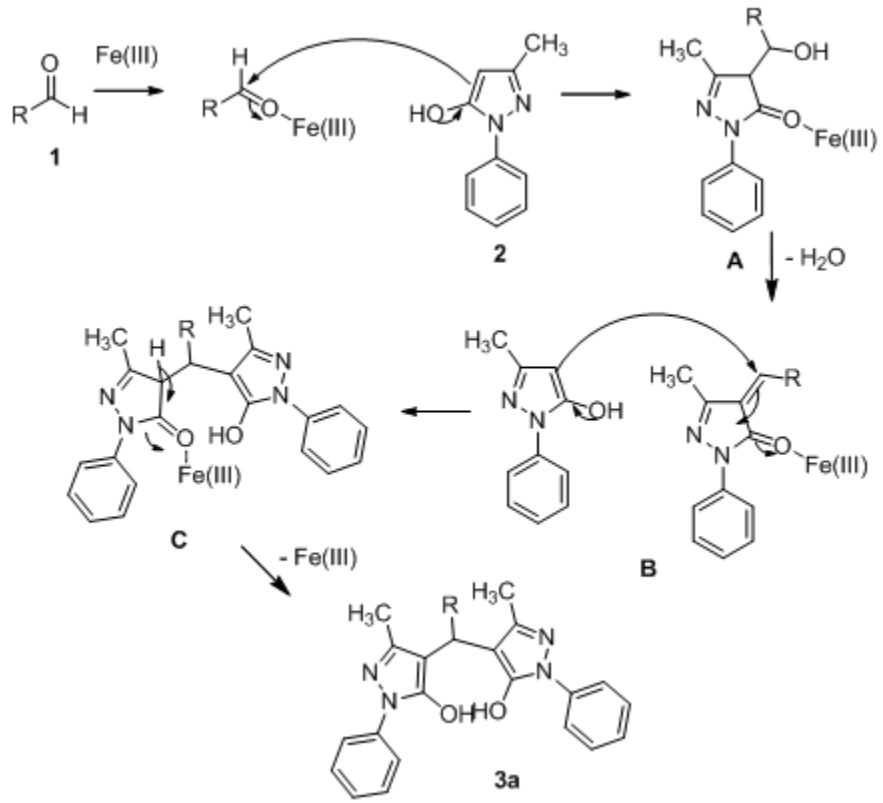
Encouraged by this success, we attempted the reaction of 3-methyl-1-phenyl-1*H*-pyrazol-5-ol with a range of other aromatic aldehydes under similar conditions (using 10 mole %, of Iron(III) chloride hexahydrate), furnishing the respective 4,4'-(phenylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) derivatives **3a-n (Scheme-1)** in excellent yields. Many of the pharmacologically relevant substitution patterns on the aromatic ring could be introduced with high efficiency. A variety of substituted aromatic aldehydes carrying electron donating or electron withdrawing substituent afforded in high yields of products with high purity.



3a) R = H; **3b**) R = 2,4-di-Cl; **3c**) R = 3-NO_2; **3d**) R = 4-CH_3; **3e**) R = 2-CH_3; **3f**) R = 2-OCH_3; **3g**) R = 3-OH; **3h**) R = 3-Cl; **3i**) R= 4-Cl; **3j**) R= 3-OCH_3; **3k**) R= 3-OPh; **3l**) R = 4-Br; **3m**) R= 2-NO_2; **3n**) R = 4-F.

Scheme. 1: Synthesis of Pyrazole derivatives (3a-n)

Based on the literature reports,[26] we have proposed the plausible mechanism for the formation of 4,4'-(phenylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) by the condensation of 3-methyl-1-phenyl-1*H*-pyrazol-5-ol (**2**) in the presence of $FeCl_3$-6H_2O **(Scheme 2)**.



Scheme. 2: Plausible mechanisam for the synthesis of pyrazole derivatives

The first step involves the formation of benzylidene **A** by the nucleophilic addition of 1-phenyl-3-methyl-5-pyrazolone to imine which formed by the reaction of aldehyde and $FeCl_3$-$6H_2O$ followed by dehydration. Then, the second molecule of 1-phenyl-3-methyl-5-pyrazolone is added to **B** in Michael addition fashion to give bis(pyrazolyl)methanes **3**.

CONCLUSION

In summary, we have developed an economically viable and eco-friendly procedure for the synthesis of 4,4'-(phenylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) derivatives with excellent yields and short reaction times which involves the use of inexpensive catalyst under water conditions makes this methodology very attractive. Furthermore, the present procedure is readily amenable to parallel synthesis and generation of combinatorial pyrazole libraries.

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EXPERIMENTAL

All the commercial reagents and solvents were used without further purification unless otherwise stated. Melting points were recorded on a Buchi 535 melting point apparatus and are uncorrected. All the reactions were monitored by thin layer chromatography performed on precoated silica gel $60F_{254}$ plates (Merck). Compounds were visualized with UV light at 254 nm and 365 nm, I_2 and heating plates after dipping in 2% phosphomolybdic acid in 15% aq. H_2SO_4 soln. IR spectra were recorded on a Perkin-Elmer 683 or a 1310 FT-IR spectrometers with KBr pellets. NMR spectra were recorded on a Varian Unity-400 MHz and BRUKER AMX 300 spectrometers using TMS as an internal standard. ^{13}C NMR was recorded on a Varian Unity 100 MHz using $CDCl_3$ as internal standard. Mass spectra were recorded on a VG Micromass 7070H and a Finnigan Mat 1020B mass spectrometers operating at 70eV.

Typical experimental procedure for the preparation of compounds 3a-h

1-phenyl-3-methyl-pyrazol-5-one (2 mmol), aromatic aldehyde (1 mmol) in water (3 mL) were mixed in a flask and $FeCl_3.6H_2O$ (10 mol %) was added at room temperature. The resulting mixture was stirred at 90°C for 30 min and completion of the reaction was monitored by TLC (ethylacetate : hexane 3:7). The reaction mixture was allowed to come to room temperature and the precipitation was isolated by filtration through a Buckner funnel and

washed with water followed by pet-ether, and then dried to give the desired product. The crude product was recrystallized from ethanol.

4,4'-(phenylmethylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) **(3a)**
Pale yellow solid. Yield: 89 % (0.388g), mp.162-165 ^{o}C. IR ; ν_{max} 3423, 3061, 2923, 1715, 1599, 1496, 1416, 1285, 1025, 755cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$); δ 7.48 (d, *J* = 7.9 Hz, 4H), 7.24 – 7.03 (m, 11H), 4.72 (s, 1H), 2.08 – 2.00 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$); δ 146.3, 140.7, 136.8, 128.7, 128.2, 127.0, 126.3, 126.1, 121.3, 33.5, 11.4. ESIMS; 438 (M+H).

4,4'-((2,4-dichlorophenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3b)
Pale yellow solid. Yield: 92 % (0.463 g), mp.170-171 ^{o}C. IR; ν_{max} 3421, 3065, 2922, 1599, 1497, 1275, 1028, 751.cm$^{-1.}$ ^{1}H NMR (500 MHz, $CDCl_3$); δ 7.67 (d, *J* = 8.5 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 4H), 7.23 – 6.98 (m, 8H), 4.91 (s, 1H), 2.02 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$); δ 146.2, 137.2, 136.6, 133.0, 132.8, 131.3, 129.1, 128.8, 126.9, 126.3, 121.4, 31.6, 11.7. ESIMS; 506 (M+H).

4,4'-((3-nitrophenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3c)
Pale yellow solid. Yield: 94 % (0.452 g), mp.170-171 ^{o}C. IR; ν_{max} 3658, 3421, 3074, 2921, 1731, 1602, 1528, 1410, 1347, 1025, 756 cm$^{-1.}$ ^{1}H NMR (300 MHz, $CDCl_3$+DMSO); δ 8.12 (s, 1H), 8.04 (d, *J* = 8.1 Hz, 1H), 7.72 (t, *J* = 7.1 Hz, 5H), 7.44 (dt, *J* = 27.8, 8.0 Hz, 5H), 7.22 (t, *J* = 7.4 Hz, 2H), 5.00 (s, 1H), 2.39 (s, 6H).^{13}C NMR (75 MHz, $CDCl_3$+DMSO); δ 147.0, 144.8, 143.0, 132.8, 128.1, 127.6, 124.7, 121.0, 120.1, 119.3, 32.8, 11.3. ESIMS; 482 ((M+H).

4,4'-(p-tolylmethylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3d)
Pale yellowsolid. Yield: 89 % (.400 g), mp.195-198^{0}C. IR; ν_{max} 3640, 3069, 2958, 2095, 1602, 1577, 1274, 756 cm$^{-1.}$^{1}H NMR (300 MHz, $CDCl_3$+DMSO); δ 7.72 (d, *J* = 7.9 Hz, 4H), 7.37 (t, *J* = 7.5 Hz, 6H), 7.20 (t, *J* = 6.2 Hz, 4H), 4.87 (s, 1H), 2.32 (s, 6H), 2.28 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO); 145.4, 137.9, 136.8, 134.7, 128.1, 128.0, 126.4, 124.8, 120.3, 32.7, 20.1, 11.1. ESIMS; 451 (M+H).

4,4'-(o-tolylmethylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3e)
Pale yellow solid. Yield: 91 % (0.410 g), mp.218-221 ^{o}C. IR; ν_{max} 3448, 3067, 2919, 1613, 1555, 1497, 1402, 1311, 834, 742 cm$^{-1.}$^{1}H NMR (300 MHz, $CDCl_3$+DMSO); δ 7.79 – 7.60 (m, 6H), 7.38 (t, *J* = 7.7 Hz, 4H), 7.26 – 7.02 (m, 4H), 4.91 (s, 1H), 2.34 (s, 6H), 2.31 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$+DMSO); δ 144.6, 138.8, 134.1, 129.6, 127.8, 127.5, 125.4, 124.7, 120.1, 31.0, 19.3, 11.1. ESIMS; 451 $(M+H)^{+}$.

4,4'-((2-methoxyphenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3f)
Pale yellow solid. Yield: 93 % (0.433 g), mp.206-209 ^{o}C. IR; ν_{max} 3416, 3065, 2918, 1712, 1598, 1496, 1241, 1022, 756 cm$^{-1.}$^{1}H NMR (300 MHz, $CDCl_3$+DMSO); δ 7.81 – 7.67 (m, 5H), 7.38 (dd, *J* = 16.0, 8.5 Hz, 4H), 7.16 (dt, *J* = 9.2, 4.4 Hz, 3H), 6.94 – 6.79 (m, 2H), 5.28 (s, 1H), 3.84 (s, 3H), 2.34 (S, *J* = 9.4 Hz, 6H).^{13}C NMR (75 MHz, $CDCl_3$+DMSO); δ 155.4, 146.0, 130.1, 128.6, 128.1, 126.7, 125.0, 120.6, 119.7, 109.6, 54.7, 27.3, 11.3. ESIMS; 467 $(M+H)^{+}$.

4,4'-((3-hydroxyphenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3g)
Pale yellow solid. Yield: 92 % (0.415 g), mp.170-171 ^{o}C. IR; ν_{max} 3420, 3065, 2924, 1599, 1496, 1282, 1023, 751 cm$^{-1.}$^{1}H NMR (300 MHz, $CDCl_3$+DMSO); δ 7.74 (d, *J* = 7.9 Hz, 4H), 7.37 (t, *J* = 7.8 Hz, 4H), 7.13 (dt, *J* = 15.7, 7.6 Hz, 3H), 6.83 – 6.60 (m, 3H), 4.86 (s, 1H), 2.33 (s, 6H).^{13}C NMR (125 MHz, $CDCl_3$+DMSO); δ 156.7, 145.8, 142.6, 128.6, 128.2, 125.1, 120.6, 117.8, 114.1, 113.0, 33.1, 11.3. ESIMS; 454 $(M+H)^{+}$.

4,4'-((3-chlorophenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3h)
Pale yellow solid. Yield: 96 % (0.451 g), mp.156-159 ^{o}C. IR; ν_{max} 3424, 3063, 2921, 1705, 1598, 1498, 1288, 751 cm$^{-1.}$^{1}H NMR (500 MHz, $CDCl_3$); δ 7.48 (d, *J* = 7.9 Hz, 4H), 7.22 (t, *J* = 7.8 Hz, 4H), 7.12 (qd, *J* = 15.0, 7.9 Hz, 6H), 4.68 (s, 1H), 2.04 (s, 6H).^{13}CNMR (125 MHz, $CDCl_3$); δ 146.1, 143.0, 136.6, 134.1, 129.5, 128.8, 127.2, 126.5, 126.3, 125.4, 121.3, 33.3, 11.4. ESIMS; 471 $(M+H)^{+}$.

4,4'-((4-chlorophenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3i)
Pale yellow solid. Yield: 92 % (0.432 g), mp.162-165 ^{o}C. IR; ν_{max} 3445, 3062, 2921, 2854, 1600, 1494, 1014, 748 cm$^{-1.}$^{1}H NMR (500 MHz, $CDCl_3$); δ 7.74 (d, *J* = 7.7 Hz, 4H), 7.43-7.10 (m, 10H), 4.88 (s, 1H), 2.35 (s, 6H).^{13}CNMR (75 MHz, $CDCl_3$+DMSO); 145.4, 143.6, 129.7, 129.2, 128.6, 128.1, 125.5, 125.2, 121.7, 120.5, 33.0, 11.3. ESIMS; 471 $(M+H)^{+}$.

4,4'-((3-methoxyphenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3j)

Pale yellow solid. Yield: 96 % (0.447 g), mp.163-166 ^{o}C. IR; ν_{max} 3442, 3038, 2920, 2558, 1807, 1715, 1594, 1490, 1407, 1288, 746 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$); δ 7.50 (m, 4H), 7.25-7.01 (m, 7H), 6.81-6.64 (m, 3H), 4.69 (s, 1H), 3.68 (d, *J* = 8.0 Hz, 3H),2.04(s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO); δ 157.2, 145.4, 133.0, 128.0, 127.6, 124.9, 120.4, 112.9, 54.5, 32.4, 11.2. ESIMS: 467 $(M+H)^+$.

4,4'-((3-phenoxyphenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3k)

Pale yellow solid. Yield: 87 % (0.459 g), mp. 159–163 ^{o}C. IR: ν_{max} (KBr): 3423,3063, 2922, 1713, 1598, 1495, 1456, 1237, 753, 690 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$); δ 7.75-7.66(d, *J* = 7.7 Hz, 5H), 7.44-7.32 (t, *J* = 7.6, 8.1 Hz, 6H), 7.31-7.12 (m, 5H), 7.08-6.91 (m,4H) 4.91 (s, 1H), 2.34 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$+ DMSO); δ 156.2, 155.9, 145.3, 143.1, 128.8, 128.6, 127.9, 127.8, 124.8, 122.1, 121.6, 120.2, 117.9, 117.6, 117.3, 115.4, 32.8, 11.0. ESIMS; 530 $(M+H)^+$

4,4'-((4-bromophenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3l)

Pale yellowsolid. Yield: 93 % (0.478 g) mp. 157-160^{0}C. IR; ν_{max} 3426, 3059, 2920, 1716, 1599, 1492, 1409, 1288, 1012, 749, 688 cm^{-1}. ^{1}H NMR (300 MHz, DMSO); δ 7.76-7.69 (d, *J* = 7.9 Hz, 4H), 7.42-7.31 (t, *J* = 7.9, 6.9 Hz, 6H), 7.24-7.15 (t, *J* = 8.1, 4.3 Hz, 4H), 4.85 (s, 1H), 2.34 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO); δ 145.5, 140.2, 130.6, 128.7, 128.2, 125.2, 120.6, 119.3, 32.8, 11.3.ESIMS: 516 $(M+H)^+$.

4,4'-((2-nitrophenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3m)

Pale yellowsolid. Yield: 95 % (0.457 g) mp. 178-182^{0}C. IR; ϑ_{max} 3066, 2922, 1715, 1599, 1499, 1413, 751, 685 cm^{-1}. ^{1}H NMR (300 MHz, DMSO); δ 8.14-8.07 (d, *J* = 8.8 Hz, 2H), 7.93-7.70 (d, *J* = 7.9 Hz, 4H), 7.56 - 7.47 (t, *J* = 10.1 Hz, 2H), 7.43-7.34 (t, *J* = 7.7 Hz, 4H), 7.26-7.17 (t, *J* = 7.3 Hz, 2H), 4.98 (s, 1H), 2.38 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO); δ 144.7, 127.6, 127.3, 124.7, 122.2, 119.9, 32.8, 10.7.ESIMS; 482 $(M+H)^+$.

4,4'-((4-fluorophenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3n)

Pale yellow solid. Yield: 92 % (0.417 g) mp. 153-157^{0}C. IR; ϑ_{max} 3065, 2922, 1713, 1599, 1500, 1456, 1429, 1366, 1290, 754, 691 cm^{-1}.^{1}H NMR (300 MHz, $CDCl_3$+DMSO); δ 7.79-7.69 (d, *J* = 7.9 Hz, 4H), 7.56-7.33 (m, 6H), 7.32 - 7.16 (m, 2H), 7.00-6.86 (m, 2H), 4.90 (s, 1H), 2.37 (s, 6H).^{13}C NMR (75 MHz, $CDCl_3$+DMSO): δ 145.3, 136.6, 128.3, 128.1, 125.0, 120.4, 114.2, 114.0, 32.5, 11.2.ESIMS; 455 $(M+H)^+$.

REFERENCES

1. Fustero S, Simón-Fuentes A and Sanz-Cervera F. Org Prep Proced Int. 2009;41:253. (b) Krasavin M and Konstantinov IO. Lett Org Chem. 2008;5:594.(c) Burguete A, Pontiki E, Hadjipavlou-Litina D, Villar R, Vicente E, Solano B, Ancizu S, Perez-Silanes S, Aldana I and Monge A. Bioorg Med Chem Lett. 2007;17:6439.
2. Castagnolo, Manetti D, Radi F, Bechi MB, Pagano M, A De Logu, Meleddu R, Saddi M and Botta M. Synthesis, biological evaluation, and SAR study of novel pyrazole analogues as inhibitors of Mycobacterium tuberculosis: Part 2. Synthesis of rigid pyrazolones. Bioorg Med Chem. 2009;17: 5716-5721.
3. Behr LC, Fusco R and Jarboe CH. in The Chemistry of Heterocyclic Compounds, Pyrazoles, Pyrazolines, Pyrazolidines, Indazoles and Condensed Rings ed by A. Weissberger, Interscience, New York. 1967;22.
4. Rosiere CE and Grossman MI. Science. 1951;113:651.
5. Pasha FA, Muddassar M, Neaz MM and Cho S. J Mol Graph Model. 2009;28:54.
6. Rosiere CE and Grossman MI. Science. 1951;113:651.
7. (a) Chauhan PMS, Singh S and Chatterjee RK. Indian J Chem Sect B. 1993;32:858. (b) Chauhan PMS, Singh S and Chatterjee RK. Indian J Chem Sect B Org Chem Incl Med Chem. 1993;32: 858.
8. Bailey DM, Hansen PE, Hlavac AG, Baizman ER, Pearl J, Defelice AF and Feigenson ME. J Med Chem. 1985;28:256.
9. Londershausen M. Pestic Sci. 1996;48:269.
10. Lubs HA. The Chemistry of Synthetic Dyes and Pigments, AmericanChemical Society, Washington, DC. 1970.
11. Singh D. J Indian Chem Soc. 1991;68:165.
12. (a) Barge M and Salunkhe R. RSC Advances. 2014; 4:31177. (b) Sara S, Elham S, Ali-Reza H and Soodabeh

R. Journal of Organometallic Chemistry. 2009;694:3027. (c) Mohammad Ali Z, Roya A and Saeed B. RSC Advances. 2015;5:71942. (d) Hamid Reza S, Mohsen S, R. Sudabeh, S. Athar, Green Chemistry. 2012, 14, 1696.
13. (a) Breslow R, Maitra U and Rideout DC. Tetrahedron Lett. 1983;24:1901. (b). Breslow R, Maitra U and Rideout DC. Tetrahedron Lett. 1984;25:1239.
14. (a) Ponaras AA. J Org Chem. 1983;48:3866. (b) Coates RM, B. D. Roagers, S. J. Hobbs, D. R. Peck, D. P. Curran, J. Am. Chem. Soc. 1987, 109, 1160.
15. (a) L. Nagarapu, V. Hanmath Reddy, C. H. Narshimahagi,; B. Rajashaker, A. R. Reddy, Synth. Commun. 2012, 42, 2131. (b) L. Nagarapu, Y. Bandi, R. Bantu, Eur. J. Med. Chem. 2014, 79, 260. (c) L. Nagarapu,; Y. Bandi,; R. Bantu, Eur. J. Med. Chem. 2014, 71, 91. (d) L. Nagarapu, H. R. Vulupala, R. Bantu, Y. Sajja, J. B. Nanubolu, Tetrahedron Asymmetry 2014, 25, 578. (e) L. Nagarapu, K Shuklachary, R. Bantu, Tetrahedron 2012, 68, 5829. (f) L. Nagarapu, M. Raghu, Y. Lingappa, Tetrahedron Lett. 2011, 52, 3401. (g) L. Nagarapu, M. Raghu, Y. Lingappa, Synlett 2011, 2730. (h) L. Nagarapu, V. Paparaju, A. Satyander, R. Bantu, Tetrahedron Lett. 2011, 52, 7075. (i) R. Bantu, H. B. Mereyala, L. Nagarapu, S. Kantevari, Tetrahedron Lett. 2011, 52, 4854. (j) L. Nagarapu, N. Ravirala, D. M. Akkewar, Synthetic Commns. 2002, 32, 2195. (k) L. Nagarapu, N. Ravirala, D. M. Akkewar, Heterocyclic Commns. 2001, 7, 237.
16. C. Bolm, J. Legros, J. L. paih, L. Zani, Chem. Rev. 2004, 104, 6217. (b) J. Bonnamour, C. Bolm, Org Lett. 2008, 10, 2655. (c) A. Correa, M. Carril, C.Bolm, Angew. Chem. Int. Ed. 2008, 47, 2880. (d) C. C. Kofink, B. Blank, S. Pagno, N. Gotz, P. Knochel, Chem Comm. 2007, 1954. (e) J. Kischel, I. jovel, K. Mertins, A. Zapf, M. Beller, Org, Lett. 2006, 8, 19.
17. R. C. Cioc, E. Ruijter, R. V. A. Orru, Green Chem. 2014, 16, 2958.
18. J. Lu, Y. Bai, Z. Wang, B. Yang, W. Li, Synth. Commun. 2001, 31, 2625.
19. J. Lu, H. Ma, Synlett. 2000, 63.
20. S. Mahajan, B. Sharma, K. K. Kapoor, Tetrahedron Lett. 2015, 56, 1915.
21. X.-S. Fan, Y.-Z. Li, X.-Y. Zhan, X.-Y. Hu, J.-J Wang. Chin. Chem. Lett. 2005, 16, 897.
22. F. Chen, M. Lei, L. Hu, Green Chem. 2014, 16, 2472.
23. D. Jariwala, V. K. Sangwan, L. J. Lauhon, T. J Marks, M. C Hersam, ACS Nano 2014, 8, 1102.
24. F. Jahani, M. Tajbakhsh, H. Golchoubian, S. Khaksar, Tetrahedron Lett. 2011, 52, 1260.
25. B. W. H Baugher, H. O. H Churchill, Y. Yang, P. Jarillo-Herrero, Nat. Nanotechnol. 2014, 9, 262.
26. S. Kuppusamy, S. Gnanamani, P. S. Nagarajan , M. Seeralan, T. P. Paramasivan, R. Melani, Bioorg. Med.Chem .Lett. 2009, 19, 4501.(b) K. R. Phatangare, V. S. Padalkar, V. D. Gupta, V. S. Patil, P. G. Umape, N. Sekhar, Synthetic Commns. 2012, 42, 1349.